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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 15/86, A61K 35/76, 39/12		A3	(11) International Publication Number: WO 95/07994
		(43) International Publication Date: 23 March 1995 (23.03.95)	
(21) International Application Number: PCT/US94/10469		(81) Designated States: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KO, KP, KR, KZ, LK, LT, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GE, GR, IE, IT, LI, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD).	
(22) International Filing Date: 15 September 1994 (15.09.94)		Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(30) Priority Data: 08/122,791 15 September 1993 (15.09.93) US 08/198,450 18 February 1994 (18.02.94) US		(88) Date of publication of the international search report: 17 August 1995 (17.08.95)	
(71) Applicant: VIAGENE, INC. [US/US]; 11055 Roselle Street, San Diego, CA 92121 (US).			
(72) Inventors: DUBENSKY, Thomas, W., Jr.; 12729 Via Felino, Del Mar, CA 92014 (US). IBANEZ, Carlos, E.; 13592 Millpond Way, San Diego, CA 92129 (US). CHANG, Stephen, M., W.; 9838 Via Cacares, San Diego, CA 92129 (US). JOLLY, Douglas, J.; 277 Hillcrest Drive, Leucadia, CA 92024 (US). DRIVER, David, A.; 5142 Biltmore Street, San Diego, CA 92117 (US). POLO, John, M.; 1222 Reed Avenue, No. 4, San Diego, CA 92109 (US).			
(74) Agents: McMASTERS, David, D. et al.; Seed and Berry, 6300 Columbia Center, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).			
(54) Title: RECOMBINANT ALPHAVIRUS VECTORS			
(57) Abstract The present invention provides composition and methods for utilizing recombinant alphavirus vectors.			

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INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US 94/10469

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/86 A61K35/76 A61K39/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Maximum documentation searched (classification system followed by classification symbols)

IPC 6 C12N A61K

Documentation searched other than maximum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J. VIROLOGY, vol. 63, no. 12, December 1989, USA pages 5216 - 5227 GRAKOUI A. ET AL. 'A cis-acting mutation in the Sindbis Virus junction region which affect subgenomic RNA synthesis' See the document in its entirety	1,4, 8-10, 21-26,29
Y	See the document in its entirety	2,3,5-7, 11-21, 27-30
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, each combination being relevant to a person skilled in the art
- "A" document member of the same patent family

Date of the actual completion of the international search:

24 March 1995

Date of mailing of the international search report

17.07.95

Name and mailing address of the ISA
European Patent Office, P.O. Box 5888 (Patentlaan 2)
NL - 2280 LV Rijswijk
Tel. (+31-78) 340-2040, Tx. 31 651 ago nl,
Fax (+31-70) 340-2016

Authorized officer

Germinario C.

INTERNATIONAL SEARCH REPORT

Int. Appl. No.
PCT/US 94/10469

(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J. VIROLOGY, vol.65, no.5, May 1991, USA pages 2501 - 2510 RAJU R. ET AL. 'Analysis of Sindbis Virus promoter recognition in vivo using novel vectors with two subgenomic mRNA promoters' See the document in its entirety	2-6, 8-10, 21-24, 26,30
Y	See document in its entirety	1,7,8, 11-20, 25,27-29
Y	--- J. VIROLOGY, vol.66, no.2, February 1992, USA pages 857 - 864 HERTZ, J. M. ET AL. 'Utilisation of heterologous alphavirus junction sequences as promoter by Sindbis virus' See Results and Material and Methods	1-30
Y	WO,A,92 10578 (BIOPTION) 25 June 1992 See page 3-13, examples 2-4, claims 12 to 41 ---	1-30
Y	SCIENCE, vol.243, 3 March 1989, WASHINGTON pages 1188 - 1191 CHENG XIONG ET AL. 'Sindbis virus: an efficient broad host range vector for gene expression in animal cells' See the document in its entirety	1-30
Y	US,A,5 091 309 (WASHINGTON UNIVERSITY) 25 February 1992 cited in the application See Summary and example 2 -----	1-30

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 94/ 10469

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

please see enclosure...!!

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-6, 29, 30 and dependent claims (i.e. 1-30)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCTISA/210

LACK OF UNITY OF INVENTION

1. Claims: 1-6, 29, 30 and claims dependent (i.e.: 1-30)
2. Claims: 31, 34 and claims dependent
3. Claims: 37, 38, 40, 44, 56, 57, 63, 72, 75-79, 84 and claims dependent
4. Claims: 85, 86 and claims dependent

The present application comprises 28 independent claims which identify four independent inventions.

The subject matter of the first invention is represented by the alpha-virus vector of claims 1 to 6, 29, 30 and claims dependent thereon. The vector is characterized by the feature of comprising a modified or inactivated viral junction region, which implies the prevention of the transcription of the subgenomic fragment and therefore the defective or blocked expression of the alpha virus structural proteins.

The subject matter of the second invention is the expression cassette of claims 31 and 34 and claims dependent thereon. The cassette comprises a promoter which directs the expression of alpha virus structural proteins. This second invention is not directed to an alpha virus vector and does not comprise the characterizing feature of the previous invention, namely a modified junction region. Should in any case this region be present in the cassette, it would be fully functional (contrary to the first invention) to allow the expression of the viral structural protein.

FURTHER INFORMATION CONTINUED FROM PCTISA/210

The subject matter of the third invention is represented by the alpha virus particles and cells infected by said particles of claims 37, 38, 40, 44, 56, 57, 63, 72, 75-79, 84 and claims dependent thereon.

The lack of unity of this invention versus the alpha vector of the first invention derives from the fact the alpha vector is not necessarily packaged into a viral particle of the third invention.

Moreover the viral particles do not comprise an inactivated or modified junction region, which is the characterizing feature of the first invention.

The fourth invention is the layered vector initiation system of claims 85, 86 and claims dependent thereon, which is in no way limited to alpha virus.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Appl. No.

PCT/US 94/10469

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9210578	25-06-92	AU-B- 656545	09-02-95
		AU-A- 9078791	08-07-92
		EP-A- 0561890	29-09-93
		JP-T- 6504198	19-05-94
US-A-5091309	25-02-92	NONE	